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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,036	03/16/2004	Stephen D. Pacetti	050623.00311	7967

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SQUIRE, SANDERS & DEMPSEY LLP
1 MARITIME PLAZA
SUITE 300
SAN FRANCISCO, CA 94111

EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
05/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/805,036	PACETTI, STEPHEN D.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *7-12,16-18,28-33 and 37-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,13-15,19-27,34-36,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

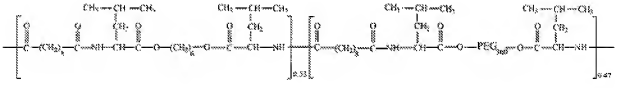
Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

To summarize the current election, applicant elected the species where the polymer is polymer 23 (depicted below) and the reagents used to produce it are compounds 1, 5, and 9.



The claims that were withdrawn from consideration are 7-12, 16-18, 28-33, and 37-39.

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

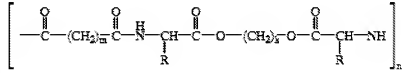
The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

Claims 1, 3-6, 13-15, 19-21, 23-27, 34-36, and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsarava et al. (previously cited) in view of Katsarava et al. (previously cited – henceforth Katsarava et al. reference B), Nagata (previously cited) and Bezemer et al. (Journal of Biomedical Materials Research 2000 52:8-17).

Claims 1, 3-6, and 13-15 recite a product-by-process. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Here the only structure conferred by the process steps of the claims is the chemical structure of the polymer in the coating. Thus the prior art need only teach or make obvious the polymer structure in the coating, regardless of the process used to produce, it in order to meet the limitations drawn to the polymeric material.

Katsarava et al. teach biodegradable poly(ester amide) polymers made from amino acids that are used to coat implantable medical devices and provide controlled

release of biologically active substances (see paragraphs 15-16, 45, and 47). In particular, the compounds are made from the polymerization of a diol (D) with a dicarboxylic acid (C) and an alpha-amino acid (A) (see paragraph 16). The resulting polymers have monomers arranged to form DACA (formula II) or CADA (formula I). In particular, poly(ethylene glycol) as well as a C_6 alkylene diol are envisioned as diols (D) (see paragraphs 10-14, 17, and 19-21; instant claims 1, 3, 13, 19-21, 24, 34, and 40-41). Leucine is envisioned as a particularly preferred amino acid (A) (see paragraphs 10-14 and 25; instant claims 1, 3-6, 13-15, 19-21, 24-27, 34-36, and 40-41). A linear C_8 α, ω dicarboxylic acid is taught as a preferred dicarboxylic acid (C) (see paragraphs 10-14, 18-19, and 22; instant claims 1, 19-21, and 40-41). A particular set of polymers with CADA configured units that were known are depicted in formula I (see below)



[0011] where

[0012] k=2, 3, 4, or 6

[0013] m=4 or 8, and

[0014] R=$CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $(CH_2)_3CH3$, $CH_2C_6H_5$, or $(CH_2)_3SCH_3$.

Katsarava et al. do not explicitly teach the elected polymer with two different CADA units such that one has poly(ethylene glycol) as the diol while the other utilizes a hexyl moiety as the diol.

Katsarava et al. reference B teaches poly(ester amide) polymers that are composed of CADA monomers and are the form of formula I (see Schemes 1-3). One particular polymer (termed 8-L-Leu-6) taught has m = 8, k=6 and R = iso-butyl thereby teaching a monomer where C is a linear C_8 α, ω dicarboxylic acid, A is leucine, and D is a C_6 alkylene (hexyl) diol (see Table II compound 10). This is one of the CADA monomers in the elected polymer. This polymer is produced by the polymerization of a monomer constructed by the condensation of an amino acid with a diol whose product is then reacted with a dicarboxylic acid (see Schemes 1 and 2; instant claims 21 and 24-27) Katsarava et al. reference B also teaches that degradation of their polymers is enzymatically catalyzed (see table VIII).

Nagata teaches that aliphatic polyesters were known degradable synthetic polymers whose degradation could be uneven due to their hydrophobicity and high melting point (see page 33 column 1 paragraph 1). Nagata also teach that the introduction of poly(ethylene glycol) (PEG) segments into the polymer backbone would solve this issue (see page 33 column 1 paragraph 1). Nagata demonstrates that the presence of a low molecular weight PEG (PEG 200) allows for degradation to occur via both a standard hydrolytic route and an enzymatically catalyzed route (see figure 4). In addition, the length of the PEG chain and the proportion of PEG in the polymer determine the polymers susceptibility to enzyme catalyzed degradation, thereby allowing one of ordinary skill to control or tune the polymer degradation to a desired end point (e.g. slower or faster) (see figure 4).

Bezemer et al. teach that the application of biodegradable amphiphilic block copolymers as drug delivery systems was known (see page 8 column 1 paragraph 1). They go on to teach the use of PEG as a hydrophilic segment in such polymers and hydrophobic blocks to create physical crosslinks that give the material its mechanical properties (see page 8 column 2 paragraph 1). Specifically, Bezemer et al. teach poly(ether ester amide) multiblock copolymers composed of poly(ester amide) blocks and poly(ether ester amide) blocks (see Scheme 2). The distinction between the two blocks in the polymer is that in one an aliphatic diol is used while in the other a PEG diol is used. Variation in the proportion of aliphatic diol to PEG controls the rate of degradation of the polymer and the rate of drug release (see page 9 column 1 paragraph 1, figures 7 and 8)

Polymers composed of CADA monomers were known at the time of the invention. In addition, the selection of a linear C_8 α, ω dicarboxylic acid for C, leucine for A, and a hexyl diol or PEG for D were specifically taught. In the case of the hexyl diol the CADA polymer is a poly(ester amide) while the case of PEG diol could be referred to as a poly(ether ester amide). In light of both Katsarava et al. and Katsarava et al. reference B, these two polymers that compose the two blocks of the elected polymer would have been obvious to one of ordinary skill in the art at the time of the invention. The elected polymer, like that of Bezemer et al., is a multiblock copolymer composed of poly(ester amide) blocks and poly(ether ester amide) blocks that differ only in the use of an aliphatic diol or PEG diol in its construction. The exchange of the aliphatic diol for a PEG diol in blocks of the polymer allows modulation of the release of drug such that the

drug release rate and degradation rate increases as the poly(ethylene glycol) proportion increases (see figures 7 and 8). Further, based upon the teachings of Nagata the integration of this PEG segment into the poly(ester amide) would be expected to confer additional avenues of enzymatic degradation *in vivo* where the resulting poly(ether ester amide) would be more susceptible to enzymatic degradation. This would have been desirable to one of ordinary skill in the art at the time of the invention to afford them greater control over the rate of drug release from a coating on a medical device. By parallel, it would have been obvious to one of ordinary skill in the art at the time of the invention to construct a polymer like that of Bezemer et al. based on the poly(ether amide)s of Katsarava et al. in view of Katsarava et al. reference B (applying a known technique to improve a similar product). This modification would be expected to provide the ordinarily skilled artisan greater control over the rate of drug release from the polymers of Katsarava et al. in view of Katsarava et al. reference B as well as mechanical integrity as taught by Bezemer et al. Taking the 8-L-Leu-6 polymer taught by Katsarava et al. reference B as the base poly(ester amide), the result of this modification is the elected polymer. It then follows that the application of this polymer to a device surface as taught by Katsarava et al. would also have been obvious.

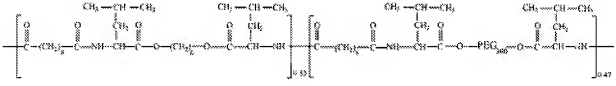
Since condensation of a diol with an amino acid was a known synthetic route for producing the diol-diamines in the CADA units and PEG was a known diol, it would have been obvious to one of ordinary skill in the art at the time of the invention to use this same route to produce the PEG-diester-diamine (a PEG version of a diol-diamine where a PEG-diester is the "diol") for the PEG containing CADA monomer unit (see

Katsarava et al. reference B scheme 1; instant claims 21 and 34). To produce the elected polymer made by obvious by the combination of both Katsarava et al. references Nagata, and Bezemer et al. there would need to be a molar amount of the dicarboxylic acid equal to the total molar amount of the diol-diamine and the PEG-diester-diamine such that each monomer unit would have one dicarboxylic acid moiety. So if X is the molar amount of diol-diamine and Y is the molar amount of PEG-diester-diamine, there would need to be X + Y moles of dicarboxylic acid (see instant claim 23). Based upon the teachings of Bezemer et al. that the proportion of PEG containing blocks in the poly(ether ester amide) controls the rate of degradation and drug release from the polymer as well as the teachings of Nagata that the longer PEG chains in the polyester result in a faster rate of enzymatic degradation (see figure 4), it would have been well within the purview of one of ordinary skill in the art to optimize such monomer/reactant proportions and PEG chain length as a matter of routine experimentation. Thus it would have been obvious to one of ordinary skill in the art to employ the elected polymer as a coating on an implantable substrate of a medical article as well as fabricate the article via the claimed method. Therefore claims 1, 3-6, 13-15, 19-21, 23-27, 34-36, and 40-41 are obvious over Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al.

Claims 1-2 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al.

as applied to claims 1, 3-6, 13-15, 19-21, 23-27, 34-36, and 40-41 above, and further in view of Michal (previously cited).

Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al. make obvious a coated medical article and its claimed method of production where the polymer coating includes the elected poly(ester amide)



Although this modified reference does teach the medical article to be one that contacts blood, it does not explicitly teach the article is a stent. Michal teaches stents with a series of polymeric coatings (see Katsarava et al. paragraph 47). In particular, Michal teaches biodegradable polymers being used as an overcoat on stents and specifically name poly(ester amide)s as envisioned polymers for such a purpose (see paragraphs 15 and 26; instant claims 2 and 22). In view of the teachings of Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al. that the poly(ester amide)s can be used in implanted devices that contact blood, it would have been obvious to one of ordinary skill in the art at the time of the invention to select a stent as one such device. Therefore claims 1-2 and 21-22 are obvious Katsarava et al. in view of Katsarava et al. reference B, Nagata, Bezemer et al., and Michal.

Response to Arguments

Applicant's arguments, filed February 12, 2010, have been fully considered but they are not deemed to be persuasive.

Regarding rejections under 35 USC 103(a) over Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al.:

Applicant argues that the combination of references does not suggest, teach or motivate a CAD_1A-CAD_2A copolymer where D_1 is an aliphatic diol and D_2 is a polyether diol. In particular, they argue that Bezemer et al. teach multi-block copolymers with a $CMCD_1$ block and $CMCD_2$ block, where M is a diamine while Katsarava et al. doe not teach a diamine. The citation of Bezemer et al. illustrates the point that the conversion of a known polyesteramide that includes an aliphatic diol unit into a block copolymer where the two blocks differ by the replacement of the aliphatic diol with a polyether diol had been done at the time of the invention. The citations of Bezemer et al. lead back to the teachings of Ciceri et al. (GB 1365952 –see claims 1, 14, and 15) that teach the $CMCD_1$ polyesteramides used as the basis for the copolymers of Bezemer et al. In addition to the teachings of Bezemer et al. of the benefits of including polyethylene glycol segments (lack of immunogenicity, solubility in organic solvents, non-toxicity) in biodegradable polymers for drug delivery, Nagata et al. teaches that the incorporation of polyethers into the backbone of polyesters evens out their degradation and allows polyester polymers to be degraded by both hydrolysis and enzymatic degradation. Such dual degradation mechanisms allow the artisan of ordinary skill more control over the

timing of drug release when using such polymer systems. Therefore by extension, one of ordinary skill in the art would also have expected the same benefits to occur if such modifications were made to the polyesteramides of Katsarava et al. since they also utilize an aliphatic diol. This artisan would have had the ability to make the elected polymer because both blocks are taught by Katsarava et al. in view of Katsarava reference B. and had a reasonable expectation of success. While applicant points at the multiblock architecture of Bezemer et al. as being different than that instantly claimed, both Katsarava et al. references, Bezemer et al. and the instant application teach a 'one pot' polycondensation of diamines with diols or diacids to prepare their final polymer. In addition, the instant specification does not explicitly recite that the polymer is a diblock. Moreover, one of ordinary skill would expect a similar polymer architecture given the same monomer proportions for the 'one pot' synthesis scheme taught by the references and the instant application.

Regarding rejections under 35 USC 103(a) over Katsarava et al. in view of Katsarava et al. reference B, Nagata, Bezemer et al., and Michal:

Applicant's arguments reiterate those made against the rejection over Katsarava et al. in view of Katsarava et al. reference B, Nagata, and Bezemer et al. Those arguments were address above and are similarly reiterated here.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated

or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615